IN THE UNITED STATES PATENT & TRADEMARK OFFICE

In re Application of:	Sándor Sipka et al.
Serial No:	10/651,136
Filed:	August 28, 2003
For:	Process for Inhibiting Allergic Disease
Art Unit:	1644
Examiner:	Nora M. Rooney

REPLY BRIEF

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

The present Reply Brief is submitted in response to the Examiner's Answer dated December 27, 2010. This response is necessary in order to counter aspects of the Examiner's position that were not previously set forth with the same focus and detail as set forth in the Answer.

Generally, Appellants note that the Examiner's Answer sets forth arguments similar to those expressed during prosecution. However, the Examiner more fully elucidates certain aspects of her argument that were less focused until this point, and Appellants are therefore compelled to further respond with similar focus.

Appellants maintain their position that the art combinations set forth by the Examiner – either Cochran or Khan, together with Previte and Baldridge – fail to teach or suggest all limitations of the claims presently subject to examination. The following table succinctly summarizes the teachings of the cited references:

Reference	Agent	Route	Frequency of dose	Mammal
Cochran	LPS	Inside nose	One time	Immature
Khan	LPS	Inside trachea	One time	Immature
Previte	IR-LPS	Inside peritoneum	One time	Adult
Baldridge	Combined MPL/antigen vaccine	Inside nose or subcutaneous injection	Weekly	Immature – mature (7-9 wks)

Cochran, Khan, and Previte teach only a one-time dose of either LPS or IR-LPS, and in each instance the dose is administered inside the animal. Baldridge teaches weekly administration of another agent, MPL, as an adjuvant in an antigen-containing vaccine, which is also administered inside the mammal.

First, none of these references teach application to the living environment or living space of the mammal. The Examiner contends that the claim terms "living environment" or "living space" are broadly interpreted to include the saline or air which is then injected into the mammals of Cochran, Khan, Previte, or Baldridge. However, instant Claim 1 recites application of IR-LPS to a living environment of a mammal. Instant Claim 10 adds the limitation of application via an aerosol spray to the living environment. These claimed routes of application are external to the mammal, whereas all art cited by the Examiner is limited to internal administration. The prefix "intra" (i.e., intraperitoneal, intranasal, intratracheal) by definition means "inside." Conversely, Appellants submit the terms "environment" and "living space" are well-understood to refer to conditions external to an organism. None of the references cited by the examiner teach a route of administration external to the organism. This claim element is wholly absent in the cited art. Indeed, the instantly claimed method is the first to

prophylactically decrease development of allergic asthma in a mammal by treating the external living environment of the mammal, rather than by administering a dose inside the mammal itself.

Second, with respect to the dosing schedule, the Examiner first asserted Baldridge for the teaching of "at least weekly" administration. Appellants submit Baldridge is limited to a teaching of weekly internal administration of a vaccine comprised of MPL (a truncated, structurally distinct derivative of LPS) combined with another antigen. Baldridge does not teach administration of LPS or IR-LPS. The Examiner now contends that dosing schedule is "an art-recognized results-effective variable which is well within the purview of those of ordinary skill in the art at the time the invention was made" such that the at least weekly dosing schedule lends no patentable import to the claimed invention.

While it is true that discovery of an optimum value of a result-effective variable in a *known process* is ordinarily within the skill of the art (*see* In re Aller, 42 CCPA 824, 220 F.2d 454, 105 USPQ 233 (1955)), optimization of a parameter not recognized as being result-effective is not prima facie obvious. In re Antonie, 559 F.2d 618, 620 (CCPA 1977). In order for a variable to be considered result-effective, one of ordinary skill in the art must be able to begin with a target result for a known process in mind and work toward achieving that result by experimentally manipulating a variable recognized as functional to achieving the target result. As noted above, the instant method is the first to address the problem of decreasing development of allergic asthma by treating the living environment of a mammal with IR-LPS. The claimed method is not found in the cited references and is therefore not a "known process" under In re Aller. Appellants submit the art cannot be said to establish any result-effective variable, including dosing schedule, for a method that was not known in the art.

Third, Appellants submit the combination of Cochran or Kahn with Previte relies on improper hindsight reasoning. The Examiner concedes that neither Cochran nor Khan teach administration of IR-LPS, and relies on Previte for that teaching, asserting that one skilled in the art would have been motivated to use the IR-LPS of Previte in the methods of Cochran or Khan because IR-LPS "should be safe and without toxic effects for use in infants and children." However, Previte reports a death rate of 3/10 adult subjects 6 days post-administration of IR-LPS.

In the Examiner's Answer, the Examiner contends that the acceptable degree of toxicity is not for Appellant to decide, and that Previte stands for the proposition that IR-LPS is safer than LPS, such that one having knowledge of Cochran or Khan would look to Previte to improve safety of the method. Nevertheless, it is well-settled that any art reference applied in a rejection under 35 U.S.C. §103(a) must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). The instantly claimed methods are prophylactic methods aimed at decreasing development of allergic asthma in immature mammals. Surely, one of ordinary skill in the art would not look to a protocol that resulted in the death of 30% of its subjects as a way to improve upon the safety of Khan or Cochran. Previte's reported death rate of 3/10 adult subjects 6 days post-administration would most certainly have guided a practitioner away from the use of IR-LPS in comparatively more fragile immature mammals. Appellants submit that one skilled in the art *having common sense* at the time of the invention would not have reasonably looked to Previte in seeking methods to more safely decrease development of allergic asthma in immature mammals – particularly given that the problem was already addressed to greater success by Cochran or Khan, from a mortality

standpoint. *Ex Parte Rinkevich et al.*, Appeal 2007-1317, decided May 29, 2007. "A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of argument reliant upon *ex post* reasoning." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 421 (2007). Applicants submit that, in modifying Cochran or Khan with Previte, the Examiner has engaged in impermissible hindsight reasoning, using the instant claims as a guide or roadmap in formulating the rejection.

CONCLUSION

It is submitted that the claims pending in the instant application are allowable. The final rejections of claims 1-3, 5, 10, 13, 17-18, and 22-25 under 35 U.S.C. §103 should be reversed. Favorable action by the Board is respectfully requested.

Respectfully submitted,

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